(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(71) Applicant (for all designated States except US): THE UNIVERSITY OF BRITISH COLUMBIA, The University of British Columbia, Carleton University, Simon Fraser University and the University of Victoria [CA/CA]; 4004 Wesbrook Mall, Vancouver, B.C. V6T 2A3 (CA).

(72) Inventors; and
(75) Inventors/Applicants (for US only): ZEISLER, Stefan, K. [DE/CA]; 3715 West 20th Avenue, Vancouver, British Columbia V6S 1E9 (CA). BUCKLEY, Kenneth, R. [CA/CA]; 3109 Trafalgar Street, Vancouver, British Columbia V6K 3V2 (CA). RUTH, Thomas, J. [US/CA]; 3547 West King Edward Avenue, Vancouver, British Columbia V6S 1M4 (CA).

(54) Title: APPARATUS AND METHOD FOR GENERATING ¹⁸F-FLUORIDE BY ION BEAMS

(57) Abstract: A system and method for producing ¹⁸F-Fluoride by using a particle beam to irradiate conversion medium in gaseous or liquid form. The irradiated conversion medium is contained in a chamber surrounded by a Fluoride adsorbing material to which the produced ¹⁸F-Fluoride adheres. The adsorption properties of the Fluoride adsorbing material are manipulated by an adsorption enhancing/decreasing element. A solvent dissolves the produced ¹⁸F-Fluoride off of the Fluoride adsorbing material while it is in the chamber. The solvent is then processed to obtain the ¹⁸F-Fluoride.

WO 02/101757 A2

APPARATUS AND METHOD FOR GENERATING ^{18}F-FLUORIDE BY ION BEAMS

Cross Reference to Related Application

This application claims priority under 35 U.S.C. §119 (e) of U.S. Provisional application
60/297,436 filed June 13th, 2001, the entire contents of which are specifically incorporated herein
5   by reference.

Field of the Invention

The present invention relates to a technique for producing ^{18}F-Fluoride from ^{18}O gas, ^{16}O
gas, ^{20}Ne, and/or compounds containing ^{18}O gas, ^{16}O gas, ^{20}Ne, such as ^{18}O-enriched water.

Background of the Invention

10   Radiation sources of short half-lives can be used for imaging biological systems if the
biological systems can absorb the non-poisonous versions of the sources. Radiation sources with
short half lives, such as ^{18}F-Fluoride, are needed to avoid radiation damage but must last long
enough to make the imaging practical.

^{18}F-Fluoride has a half-life of about 109.8 minutes and is not chemically poisonous in
15   tracer quantities. Fluoro-deoxyglucose (FDG) is an example of a radiation tracer compound
incorporating ^{18}F-Fluoride. In addition to FDG, compounds suitable for labeling with ^{18}F-Fluoride
include, but are not limited to, Fluoro-thymidine (FLT), fluoro analogs of fatty acids, fluoro
analogs of hormones, linking agents for labeling peptides, DNA, oligo-nucleotides, proteins, and
amino acids. ^{18}F has, therefore, many uses in forming medical and radiopharmaceutical products.
20   One use is as a radiation tracer compound for medical Positron Emission Tomography (PET)
imaging.

The isotope ^{18}F-Fluoride can be created by irradiation of targets by nuclear beams (e.g.,
protons, deuterons, alpha particles,...,etc). ^{18}F-Fluoride forming nuclear reactions include, but are
not limited to, ^{20}Ne(d,α)^{18}F (a notation representing ^{20}Ne absorbing a deuteron resulting in ^{18}F and
25   an emitted alpha particle), ^{16}O(α,pn)^{18}F, ^{16}O(^{3}H,n)^{18}F, ^{16}O(^{3}He,p)^{18}F, and ^{18}O(p,n)^{18}F; with the
greatest yield of ^{18}F production being obtained by the ^{18}O(p,n)^{18}F reaction because it has the largest
cross-section. Several elements and compounds (including Neon, water, and Oxygen) are used as
the initial material in obtaining ^{18}F-Fluoride through nuclear reactions.

Technical and economic considerations are critical factors in choosing an ^{18}F-Fluoride
30   producing system. Because the half-life of ^{18}F-Fluoride is about 109.8 minutes, quantity production

is time dependent. Thus, ^{18}F-Fluoride producers prefer nuclear reactions that have a high cross-section (i.e., having high efficiency of isotope production) to quickly produce large quantities of ^{18}F-Fluoride. Additionally, users of ^{18}F-Fluoride prefer to have an ^{18}F-Fluoride producing facility near their facilities so as to avoid losing a significant fraction of the produced isotope during

5   transportation. Production efficiency and rate are also a function of the energy and the current of the nuclear beam used for production.

One type of nuclear beam is the proton beam. Systems that produce proton beams are less complex, as well as simpler to operate and maintain, than systems that produce other types of beams. Technical and economic considerations, therefore, drive users to prefer ^{18}F-Fluoride

10   producing systems that use proton beams and that use as much of the power output available in the proton beams. Economic considerations also drive users to efficiently use and conserve the expensive startup compounds.

However, inherent characteristics of ^{18}F-Fluoride and the technical difficulties in implementing ^{18}F-Fluoride production systems have hindered reducing the cost of preparing [18]F-

15   Fluoride. Existing approaches that use Neon as the startup material suffer from problems of inherent low nuclear reaction yield and complexity of the irradiation facility. The yield from Neon reactions is about half the yield from $^{18}O(p,n)^{18}F$. Moreover, using Neon as the startup material requires facilities that produce deuteron beams, which are more complex than facilities that produce proton beams. Using Neon as the start-up material, therefore, has resulted in low ^{18}F-Fluoride

20   production yield at a high cost.

Existing approaches that use ^{18}O-enriched water (hereinafter [18]water) as the startup material suffer from problems of recovery of the unused ^{18}O-enriched water and of the limited beam intensity (energy and current) handling capability of water. Recovering the unused ^{18}O-enriched water is problematic, moreover, because of contaminating by-products generated as a result of the

25   irradiation and chemical processing. This problem has led users to distill the water before reuse and, thus, implement complex distilling devices. These recovery problems complicate the system, and the production procedures, used in ^{18}O-enriched water based ^{18}F-Fluoride generation; the recovery problems also lower the product yield due in part to non-productive startup material loss and isotopic dilution.

30   Moreover, although proton beam currents of over 100 microamperes are presently available, ^{18}O-enriched water based systems are not reliable when the proton beam current is greater than about 50 microamperes because water begins to vaporize and cavitate as the proton beam current is increased. The cavitation and vaporization of water interferes with the nuclear

reaction, thus limiting the range of useful proton beam currents available to produce ^{18}F-Fluoride from water. See, e.g., Heselius, Schlyer, and Wolf, Appl. Radiat. Isot. Vol. 40, No. 8, pp 663-669 (1989). Systems implementing approaches using ^{18}O-enriched water to produce ^{18}F-Fluoride are complex and difficult. For example, recent publications (see, e.g., Helmeke, Harms, and Knapp,
5   Appl. Radiat. Isot. 54, pp 753-759 (2001), (hereinafter "Helmeke") show that it is necessary to use a complicated proton beam sweeping mechanism, accompanied by the need to have bigger target windows, to increase the beam current handling capability of an ^{18}O-enriched water system to 30 microamperes. In spite of the complicated irradiation system and target designs, the Helmeke approach has apparently allowed operation for only 1 hour a day. Most producers of large
10 quantities of ^{18}F-fluoride use water targets with overpressure to retard boiling, and operate in the 40-50 microamperes range and are able to produce 1-3 Curies. Using water as the startup material, therefore, has also resulted in low ^{18}F-Fluoride production yield at high cost.

Target systems are critical in determining the efficiency and productivity of ^{18}F-Fluoride production. A well-designed target system can allow the efficient use of ^{18}water and ^{18}Oxygen.
15 ^{18}F-Fluoride can react with the internal surfaces of the target material reducing the extracted yield of reactive Fluoride. For example, titanium is virtually inert but difficult to cool at high beam currents (titanium targets generate ^{48}V) and silver forms colloids that can trap ^{18}F-Fluoride (silver targets form ^{109}Cd). The use of Niobium produces low concentrations of ^{93m}Mo ($T_{1/2}$ = 6.9 h) as a contaminant. All these metals can be removed via the ion column trapping. A target material will
20 need to have such properties that the removal of the ^{18}F-Fluoride accumulation on the target is unobstructed. Therefore, important considerations for successful target design include the startup material, the adsorbing target material, the layer size of the startup material exposed to the nuclear beam, the selection of chamber materials and cooling of the chamber. Glassy carbon and glassy quartz have many desirable and similar characteristics for adsorbing material. Glassy carbon is
25 temperature resistant, inert to corrosive media, and ^{18}F-Fluoride can be removed more readily from glassy carbon than from regular glassware. Glassy carbon must be cooled since rapid oxidation of glassy carbon occurs above 500°C.

Accordingly, a better, more efficient, and less costly target system and method for producing ^{18}F-Fluoride is needed.

30 Summary of the Invention

The invention presents an approach that produces ^{18}F-Fluoride by using a proton beam to irradiate ^{18}Oxygen or ^{18}water (H$_2$ ^{18}O) in gaseous, liquid or steam form. The irradiated ^{18}Oxygen or ^{18}water are contained in a chamber that includes at least one accumulation component to which the

produced ^{18}F-Fluoride adheres. A solvent dissolves the produced ^{18}F-Fluoride off of the at least one component while it is in the chamber. The solvent is then processed to obtain the ^{18}F-Fluoride.

The inventive approach has an advantage of obtaining ^{18}F-Fluoride by using a proton beam to irradiate ^{18}Oxygen or ^{18}water in gaseous, liquid or steam form. The yield from the inventive
5   approach is high when using ^{18}Oxygen because the nuclear reaction producing ^{18}F-Fluoride from ^{18}Oxygen has a relatively high cross section. The inventive approach also has an advantage of allowing the conservation of the unused ^{18}Oxygen and its recycled use. The inventive approach is not limited by the presently available proton beam currents (of existing PET cyclotrons); the inventive approach is working at beam currents well over 100 microamperes for ^{18}Oxygen. The
10   inventive approach, therefore, permits using higher proton beam currents and, thus, further increases the ^{18}F-Fluoride production yield. The inventive approach has a further advantage of producing pure ^{18}F-Fluoride, without the other non-radioactive Fluorine isotopes (e.g., ^{19}F). The inventive approach also has the advantage of using ^{18}water at lower proton beam currents. The inventive approach reduces the adherency of ^{18}F-Fluoride to the accumulation component by using
15   voltage differences and/or by heating the accumulation component during ^{18}F-Fluoride extraction, thus, increasing the ^{18}F-Fluoride production yield. The inventive approach allows cooling of the accumulation component reducing the oxidation and allowing the use of non-reactive materials such as glassy carbon.

Brief Description of the Drawings

20   Other aspects and advantages of the present invention will become apparent upon reading the detailed description and accompanying drawings given hereinbelow, which are given by way of illustration only, and which are thus not limitative of the present invention, wherein:

Figure 1 is a cross-section view of an ^{18}F generating apparatus illustrating an exemplary embodiment of a system according to the present invention; and

25   Figure 2 is a general flow chart illustrating a method of using the embodiment of Figure 1 to produce ^{18}F-Fluoride from ^{18}Oxygen gas or ^{18}water.

Detailed Description of the Preferred Embodiments

The invention presents an approach that produces ^{18}F-Fluoride by using a proton beam to irradiate ^{18}Oxygen or ^{18}water (H_2^{18}O) in gaseous, liquid or steam form. The irradiated ^{18}Oxygen or
30   ^{18}water is contained in a chamber that includes at least one accumulation component to which the produced ^{18}F-Fluoride adheres. A solvent dissolves the produced ^{18}F-Fluoride off of the at least one component while it is in the chamber. The solvent is then processed to obtain the ^{18}F-Fluoride.

Figure 1 is a diagram illustrating an exemplary embodiment of a system according to the inventive concept. As shown, an ion beam enters the ^{18}F-Fluoride generating system 100 through a region 110 of connecting tube 120, connecting tube 120 being connected to block 130. Block 130 contains two foils 130a and 130b at either end of the block 130 aperture defining a region 140. Region 140 may contain a coolant medium which enters and exits the region through an inlet and an outlet respectively (not shown). The beam traverses through region 140 into a region 160 within a flange 170. The flange 170 has at least one inlet 180 to introduce a conversion medium (e.g., ^{18}Oxygen, and ^{18}water) and/or the cleaning/removing agent into the second region 160 and the target chamber (chamber) 190. A Fluoride-18 adsorbing (adhering) material 200 (e.g., glassy carbon) forms the target chamber 190 and is cooled by coolant flowing in a cooling jacket 210 which surrounds the adsorbing material 200. The flange 170, block 130, and the connecting tube 120 are sealed with o-rings 220, 230, 300, and 310.

In the embodiment of Figure 1, the connecting tube 120 conducts an ion beam from an accelerator (not shown) to the target chamber 190. In one implementation the connecting tube is made of Aluminum. Alternative implementations for the material of the connecting tube 120 include, but are not limited to, tungsten, tantalum, or carbon. Preferably the characteristics of the material used to make the connecting tube 120 is neither transparent to the beam, nor rendered radioactive by it; thus keeping the beam from contaminating the environment outside the target chamber and aiding to keep the beam profile constant. In one implementation, the connecting tube 120 has an inside diameter 1-cm, but generally the inside diameter of the connecting tube depends on the diameter of the ion beam directed toward the target.

In the embodiment of Figure 1, the two foils 130a and 130b define a region 140. The foils are used to separate region conditions (e.g., pressures and region mediums). The two foils, 130a and 130b, can be cooled by a coolant medium in region 140, for example an inert gas allowing thinner foils, which disturb the ion beam, profile less. . Consequently thin foils and materials such as aluminum, and HAVAR® (Cobolt-Nickel alloy) can be used. Since it is not necessary that region 140 be maintained at high pressures with respect to region 110, an aluminum foil can preferably be used between connecting tube 120 and block 130. However, since higher pressures may exist between region 140 and region 160, the foil between block 130 and flange 170 is preferably made of HAVAR®. HAVAR® is preferable because it has higher mechanical strength and thus withstands, per thickness unit, relatively higher pressures than most other materials suitable for use as a foil. Consequently, a HAVAR® thin foil holds the region 140 pressure yet does not significantly reduce incident ion beam energy or intensity. Alternatively instead of HAVAR®, other suitable materials can be used as the foils 130a and 130b.

In the embodiment of Figure 1, flange 170 is preferably connected to block 130 and the adsorbing material 200. Flange 170 preferably has at least one inlet 180 to introduce the ^{18}Oxygen or ^{18}water into the volume surrounded by the adsorbing material 200. Inlet 180 is also preferably used to introduce the cleaning/removing agent (e.g., water), which removes the Fluoride-18 adhered to the adsorbing material 200, after ion beam irradiation is stopped. In alternate implementations, plural inlets 180 are used to introduce the ^{18}Oxygen or the ^{18}water and/or the cleaning/removing agent into the target chamber 190, or to take any or all of them out of the target chamber 190. The material chosen as forming flange 170 is preferably not reactive with Fluoride. In one implementation, stainless steel is used as the material forming the flange 170. In alternative implementations, niobium or molybdenum is used as the material forming flange 170.

In the embodiment of Figure 1, in an implementation, a cooling jacket 210 is used to cool the Fluoride-18 adsorbing material 200 during exposure to the ion beam; the cooling jacket in this implementation enclosing a space between itself and the Fluoride-18 adsorbing material 200. Preferably, the cooling jacket 210 has at least one inlet 240 that allows the circulation of the cooling material in the space between the cooling jacket 210 and the Fluoride-18 adsorbing material 200. In another implementation, the cooling jacket 210 has two inlets 240, one inlet for introducing the cooling fluid and the other inlet for taking out the cooling fluid; the cooling fluid thus being able to circulate between the cooling jacket 210 and the Fluoride-18 adsorbing material 200.

In an implementation, aluminum is used as the material forming the cooling jacket 210. In another non-limiting implementation, stainless steel is used as the material forming the cooling jacket 210. In a implementation, the cooling jacket 210 is made of several pieces that are attached together. In another implementation, the cooling jacket is made of one piece.

In an alternative implementation, the cooling jacket 210 is designed to come in direct contact with the Fluoride-18 adsorbing material 200, the jacket completely including a cooling device (e.g., water as circulating cooling fluid). In this implementation, the cooling device cools the cooling jacket 210, which in turn cools the coolant in the cooling jacket 210, which in turn cools the Fluoride-18 adsorbing material 200 by contact.

In an implementation, the cooling jacket 210 is used to heat the material 200 during exposure to the cleaning/removing agent, and thus aids in removing the Fluoride-18 adhered to the adsorbing material 200 by heating the material 200.

The temperature of the various parts of the target chamber 190 can preferably be monitored by, for example, thermocouple(s) (not shown in Fig. 1). Using a cooling jacket allows the cooling

of the chamber at various stages of producing ^{18}F-Fluoride. Heating tapes (not shown) may be used independently of the cooling jacket to heat the chamber or the cooling jacket may be used itself as a heating system by circulating heated fluid. Using heating tapes and/or a heating jacket allows the heating of the chamber at the various stages of producing ^{18}F-Fluoride. The cooling jacket, the

5   heating tapes, or both, can be used to control the temperature of the chamber 190. Instead of a cooling jacket and heating tapes, other cooling and heating devices can be used. The cooling and heating devices can be located inside or outside the chamber wall (adsorbing material 200). Using temperature-measuring device(s) permits and augments the tracking and automation of the various stages of the ^{18}F-Fluoride production.

10   In the embodiment of Figure 1, in an implementation, the Fluoride adsorbing material 200 has a separate heating jacket (not shown) that heats the material 200 during exposure to the cleaning/removing agent. In one exemplary implementation, heating wire/tape (or wires) is used to heat the adsorbing material 200 and thus aid in removing the Fluoride-18 adhered to the adsorbing material 200. In an implementation, the heating jacket is in direct contact with adsorbing material

15   200. In an alternate implementation, the heating jacket is in contact with the cooling jacket 210 (but not in contact with the adsorbing material 200) and effectively heats the material 200 by heating the cooling jacket 210.

In an implementation, the Fluoride adsorbing material 200 is connected to an electrical potential source (not shown in Fig. 1) that charges the material 200 with electric charges. In this

20   implementation, preferably care is taken to preserve the electrical integrity of the system by proper insulation so that the system elements, the environment, and personal are protected from exposure to undesired electrical charges. The electrical potential source allows charging the adsorbing material 200 by an electrical potential that has an opposite sign to the charge of the Fluoride-18 ion during exposure to the ion beam, thus aiding through electrical charge attraction the adsorption of

25   the formed Fluoride-18 ions to the surface of the adsorbing material 200. On the other hand, during exposure to the cleaning/removing agent, the charging system can be used so as to charge the adsorbing material 200 to an electrical potential having the same sign of the Fluoride-18 ion, thus aiding through electrical charge repulsion the desorption of the formed Fluoride-18 ions from the adsorption material 200.

30   In the embodiment of Figure 1, the Fluoride-18 adsorbing material 200 is, preferably, mechanically supported and aligned with respect to the connecting tube 120 by an alignment block 250, a washer/spring 260 and an end block 270. The alignment block 250 is preferably implemented using aluminum, copper, or VESPEL® (a form of plastic), or other suitable radiation-hard material. The washer/spring 260 is preferably implemented using Belleville Washer(s) and

end block 270 is preferably implemented using aluminum. Preferably, the various components of the target system are held together using screws (e.g., 280 and 290) or other mechanical (or chemical, e.g., glue) tools for holding materials together. Preferably, O-rings (300, 220, 230, and 310; preferably implemented as polyether./rubber or other malleable material including metals) are

5   used where appropriate to allow for mechanical flexibility (e.g., expansion due to heating and/or high pressures; contraction during cooling and/or low pressure; and vibration) and to protect non-leaking integrity.

In the embodiment of Figure 1, in an implementation, glassy carbon is used as the material forming the Fluoride-18 adsorbing material 200. For example, glassy carbon (as SIGRADUR®)

10   obtained from Sigri Corporation in Bedminster, NJ, can be used as the Fluoride adsorbing material 200. In an implementation, the glassy carbon material is in contact with the cooling jacket, or the heating jacket, or both. In another implementation, the glassy. carbon is in contact with a highly thermally conducting substrate (e.g., a layer of synthetic diamond or other appropriate material such as a metal or metallic alloy) which is then operatively in contact with the cooling and/or

15   cooling jacket(s).

In another implementation, glassy quartz is used as the material forming the Fluoride-18 adsorbing material 200. In an implementation the glassy quartz material is in contact with the cooling/heating jackets. In another implementation, the glassy quartz is in contact with a highly thermally conducting substrate (e.g., a layer of carbon as SiC, a layer of synthetic diamond, or other

20   appropriate material such as a metal or metallic alloy), which is then operatively in contact with the cooling and/or cooling jacket(s).

In another implementation, niobium is used as the material forming the Fluoride-18 adsorbing material 200. In an implementation the niobium material is in contact with the cooling jacket, or the heating jacket, or both. In another implementation, the niobium is in contact with a

25   highly thermally conducting substrate (e.g., a layer of synthetic diamond, or other appropriate material such as a metal or metallic alloy) which is then operatively in contact with the cooling and/or cooling jacket(s).

In another implementation, molybdenum is used as the material forming the Fluoride-18 adsorbing material 200. In an implementation the molybdenum material is in contact with the

30   cooling jacket, or the heating jacket, or both. In another implementation, the adsorbing material 200 is composed of a conducting substrate (e.g., a layer of synthetic diamond, or other appropriate material such as a metal or metallic alloy) operatively in contact with the cooling and/or cooling jacket(s), and a layer of molybdenum deposited on the conducting substrate facing the chamber

8

190.

In another implementation, synthetic diamond is used as the material forming the Fluoride-18 adsorbing material 200. In an implementation the synthetic diamond is in contact with the cooling jacket, or the heating jacket, or both. In another implementation, the adsorbing material 200 is composed of a conducting substrate (e.g., a metal, metallic alloy or other suitable material such as Ag, Stainless Steel (SS), etc...) operatively in contact with the cooling and/or cooling jacket(s), and a layer of synthetic diamond deposited on the conducting substrate facing the chamber 190.

Adsorbing materials include, but are not limited to, stainless steel, glassy Carbon, Titanium, Silver, Gold-Plated metals (such as Nickel), Niobium, HAVAR®, Aluminum, and Nickel-plated Aluminum.

In the embodiment of Figure 1, the target chamber 190, filled with ^{18}Oxygen gas as the material being irradiated with the ion beam, has a cylindrically shaped volume. In an alternative implementation, for using ^{18}Oxygen gas, the volume of chamber 190 has a conical shape flaring out as one goes away from the connecting tube 120.

In the embodiment of Figure 1, an implementation for using ^{18}water as the material being irradiated with ion beams to produce Fluoride-18, the volume of chamber 190 has a cylindrical shape. In an alternative implementation for using ^{18}water, volume of chamber 190 has a spherical shape. In an alternative implementation for using ^{18}water, the volume of chamber 190 has a conical shape flaring out as one goes away from the connecting tube 120.

The size of the target chamber 190 and its dimensions depend on the ion beam profile/intensity/energy, the material used (^{18}Oxygen gas or ^{18}water), its pressure, its temperature, and the desired output of Fluoride-18. It is to be noted that although this disclosure has described a target system for using ^{18}Oxygen gas or ^{18}water as the material being irradiated with ions to produce Fluoride-18, the target system described herein can be used for other methods of producing Fluoride-18 including, but not limited to, ^{20}Ne(d,α)^{18}F (a notation representing a ^{20}Ne absorbing a deuteron resulting in ^{18}F and an emitted alpha particle), ^{16}O(α,pn)^{18}F, ^{16}O(^{2}H,n)^{18}F, and ^{16}O(^{3}He,p)^{18}F.

A method of implementing the inventive concept is described hereinafter, by reference to FIG. 2, as an exemplary method for using the embodiment of FIG. 1.

In step S1010, the target chamber 190 is evacuated. This can be accomplished, for example, by opening inlet 180 and exposing the target chamber 190 to a vacuum pump (not shown). The vacuum pump can be implemented, for example, as a mechanical pump, diffusion

9

pump, or both. The desired level of vacuum in target chamber 190 is preferably high enough so that the amount of contaminants is low compared to the amount of ^{18}F-Fluoride formed per run. Heating the target chamber 190, so as to speed up its pumping, can augment step S1010.

In step S1020, the target chamber 190 is filled with a conversion substance (e.g., ^{18}Oxygen gas or ^{18}water) to a desired pressure. This can be accomplished, for example, by opening inlet 180 and allowing the conversion substance to go from a reservoir (not shown) to the target chamber 190. Pressure gauges (not shown) can be used to keep track of the pressure and, thus, the amount of conversion substance in the target chamber.

In step S1030, the conversion substance in target chamber 190 is irradiated with a proton beam. This can be accomplished, for example, by closing inlet 180 and directing the proton beam through regions 110, 140 and 160 respectively into the target chamber 190. The foils separating the target chamber from region 140 can be made of a thin foil material that transmits the proton beam while containing the conversion substance and the formed ^{18}F-Fluoride. As the proton beam is irradiating the conversion substance, some of the conversion substance nuclei undergo a nuclear reaction and are converted into ^{18}F-Fluoride. The nuclear reaction that occurs for ^{18}Oxygen is:

$$^{18}\text{Oxygen} + \text{p} \rightarrow {}^{18}\text{F} + \text{n}.$$
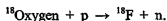
The irradiation time can be calculated based on well-known equations relating the desired amount of ^{18}F-Fluoride, the initial amount of conversion substance present, the proton beam current, the proton beam energy, the reaction cross-section, and the half-life of ^{18}F-Fluoride. TABLE 1 shows the predicted yields for a proton beam current of 100 microamperes at different proton energies and for different irradiation times using ^{18}Oxygen gas as the conversion substance.

TABLE 1

Ep(MeV)	TTY at Sat (Ci)	TTY with 2-Hour Irradiation (Ci)	TTY with 4-Hour Irradiation (Ci)
12	21	10.5	15.8
15	25	12.5	18.8
20	30	15	22.5
30	46	23	34.5

TTY is an abbreviation for thick target yield, wherein the [18]Oxygen gas being irradiated is thick enough—i.e., is at enough pressure—so that the entire transmitted proton beam is absorbed by the [18]Oxygen. The yields are in curie. TTY at Sat is the yield when the irradiation time is long enough for the yield to saturate—about 12 hours for ^{18}F production, the point where the rate of production equals the rate of radioactive decay.

Preferably the [18]Oxygen gas is at high pressures: The higher the pressure the shorter the necessary length for the target chamber 190 to have the [18]Oxygen gas present a thick target to the proton beam. TABLE 2 shows the stopping power (in units of gm/cm²) of Oxygen for various incident proton energies and ranges of penetration. The length of [18]Oxygen gas (the gas being at a specific temperature and pressure) that is necessary to completely absorb a proton beam at a specific energy is given by the stopping power of Oxygen divided by the density of [18]Oxygen gas (the density being at the specific temperature and pressure). Using this formula, a length of about 156 centimeters of [18]Oxygen gas at STP (300K temperature and 1 atm pressure) is necessary to completely absorb a proton beam having energy of 12.0 MeV. By increasing the pressure to 20 atm, the necessary length at 300K becomes about 7.75 centimeters.

TABLE 2

Proton Energy	Range	Stopping Power for [18]O
MeV	R (mm)	R(gm/cm2)
2	71.29	0.01019447
2.25	86.63	0.01238809
2.5	103.26	0.01476618
2.75	121.14	0.01732302
3	140.27	0.02005861
3.25	160.6	0.0229658
3.5	182.14	0.02604602
3.75	204.86	0.02929498
4	228.75	0.03271125
4.5	279.96	0.04003428
5	335.7	0.0480051
5.5	395.9	0.0566137
6	460.49	0.06585007
6.5	529.39	0.07570277
7	602.56	0.08616608
8	761.32	0.10886876
9	936.59	0.13393237
10	1130	0.16159
11	1340	0.19162
12	1560	0.22308
13	1800	0.2574
14	2050	0.29315
15	2320	0.33176
16	2600	0.3718

17	2900	0.4147
18	3210	0.45903
20	3880	0.55484
22.5	4790	0.68497
25	5790	0.82797
27.5	6870	0.98241
30	8040	1.14972
32.5	9280	1.32704
35	10610	1.51723
37.5	12010	1.71743
40	13490	1.92907
45	16680	2.38524
50	20160	2.88288
55	23930	3.42199
60	27970	3.99971
65	32290	4.61747
70	36880	5.27384
80	46810	6.69383
90	57750	8.25825
100	69630	9.95709

Consequently in one implementation, the target chamber 190 (along with its parts) is designed to withstand high pressures, especially since higher pressures become necessary as the target chamber 190 and gas heat up due to the irradiation by the proton beam. As one exemplary implementation of the inventive concept to produce ^{18}F-Fluoride from ^{18}Oxygen gas, we have demonstrated the success of using HAVAR® with thickness of 40 micrometers to contain ^{18}Oxygen at fill pressure of 20 atm irradiated with 13 MeV proton beam (protons with 12.5 MeV transmitting into the chamber volume, 0.5 MeV being absorbed by the HAVAR® chamber window) at a beam current of 20 microamperes. The exemplary implementation successfully contained the ^{18}Oxygen gas during irradiation with the proton beam and, therefore, with the ^{18}Oxygen gas having much higher temperatures (well over 100°C) and pressures than the fill temperature and pressure before the irradiation. In another exemplary implementation, cooling jackets (lines) were used to remove heat from the chamber volume during irradiation. An implementation would run the inventive concept at high pressures to have relatively short chamber length. In alternative implementations, other suitable designs can be used to contain the ^{18}Oxygen gas at desired pressures.

The ^{18}F-Fluoride adheres to the adsorbing material 200 as it is formed. Preferably the adsorbing material 200 is chosen to be a material to which ^{18}F-Fluoride adheres well. Additionally it is preferably one of which the adhered ^{18}F-Fluoride dissolves easily when exposed to the appropriate solvent. Such materials include, but are not limited to, stainless steel, glassy Carbon, glassy quartz, Titanium, Silver, Gold-Plated metals (such as Nickel), Niobium, HAVAR®, and Nickel-plated Aluminum. Periodic pre-fill treatment of the adsorbing material 200 can be used to enhance the adherence (and/or subsequent dissolving, see later step S1050) of ^{18}F-Fluoride.

In step 1040, the unused portion of conversion substance is removed from the target chamber 190. This can be accomplished, for example, by opening the inlet 180, inlet 180 being connected to a container (not shown), with the container cooled to below the boiling point of the conversion substance. In this case, the unused portion of conversion substance is drawn into the container and, thus, is available for use in the next run. This step allows for the efficient use of the conversion substance. It is to be noted that the cooling of the container to below the boiling point of conversion substance can be performed as the target chamber 190 is being irradiated during step S1030. Such an implementation of the inventive concept reduces the run time as different steps are performed. The pressure of the conversion substance can be monitored by pressure gauges (not shown).

In step S1050, the formed ^{18}F-Fluoride adhered to the adsorbing material 200 is preferably dissolved using a solvent without taking the adsorbing material 200 out of the target chamber 190. This can be accomplished, for example, by opening inlet 180 and allowing the solvent to be introduced to the target chamber 190. The adhered ^{18}F-Fluoride is preferably dissolved by and into the introduced solvent. Heating the target chamber 190 so as to speed up the dissolving of the produced ^{18}F-Fluoride can augment step S1050. The solvent may be introduced into the target chamber 190 by opening inlet 180 after step 1040. This procedure allows the solvent to be sucked into the vacuum existing in the target chamber 190, thus aiding in introducing the solvent and physically washing the adsorbing material 200. Alternatively, the solvent can also be introduced due to its own flow pressure.

The material used as a solvent, preferably should easily remove (physically and/or chemically) the ^{18}F-Fluoride adhered to the adsorbing material 200, yet preferably easily allow the uncontaminated separation of the dissolved ^{18}F-Fluoride. It also preferably should not be corrosive to the system elements with which it comes into contact. Examples of such solvents include, but are not limited to, water in liquid and steam form, acids, and alcohols. ^{19}Fluorine is preferably not the solvent--the resulting mixture would have ^{18}F-^{19}F molecules that are not easily separated and would reduce, therefore, the yield of the produced ultimate ^{18}F-Fluoride based compound.

TABLE 3 shows the various percentages of the produced ^{18}F-Fluoride extracted using water at various temperatures. It is seen that an adsorbing component made from Stainless Steel yields 93.2% of the formed ^{18}F-Fluoride in two washes using water at 80°C. Glassy Carbon, on the other hand, yields 98.3% of the formed ^{18}F-Fluoride in a single wash with water at 80°C, the wash time was on the order of ten seconds. Using water at higher temperatures is expected to improve the yield per wash. Steam is expected to perform at least as well as water, if not better, in dissolving the formed ^{18}F-Fluoride. Other solvents may be used instead of water, keeping in mind the objective of

rapidly dissolving the formed ^{18}F-Fluoride and the objective of not diluting the Fluorine based ultimate compound.

TABLE 3

Material of Chamber Component	% Recovered in 1st Wash	% Recovered in 2nd Wash	Total % Recovered in 2 Washes	Wash Temp °C
Ni-plated Al	66.4	7.4	73.8	80
Ni-plated Al	42.9	6.8	49.7	60
Ni-plated Al	34.4	4.4	38.8	20
Stainless Steel	80.6	12.6	93.2	80
Aluminum	5.6	1.8	7.5	80
Glassy Carbon	64.1	22.9	87.0	20
Glassy Carbon	98.3	N.A.	98.3	80

In step 1060, the formed ^{18}F-Fluoride is separated from the solvent, which can be accomplished, for example, by a separator (not shown). The separator separates the formed ^{18}F-Fluoride from the solvent and retains the formed ^{18}F-Fluoride.

The separator [not shown] can be implemented using various approaches. One implementation for the separator is to use an Ion Exchange Column that is anion attractive (the formed ^{18}F-Fluoride being an anion) and that separates the ^{18}F-Fluoride from the solvent. For example, Dowex IX-10, 200-400 mesh commercial resin, or Toray TIN-200 commercial resin, can be used as the separator. Yet another implementation is to use a separator having specific strong affinity to the formed ^{18}F-Fluoride such as a QMA® Sep-Pak, for example. Such implementations for the separator preferentially separate and retain ^{18}F-Fluoride but do not retain the radioactive metallic byproducts (which are cations) from the solvent, thus retaining a high purity for the formed radioactive ^{18}F-Fluoride. Another implementation for the separator is to use a filter retaining the formed ^{18}F-Fluoride.

In step 1070, the separated ^{18}F-Fluoride is processed from the separator. This can be accomplished, for example, by the use of an Eluent to separate the ^{18}F-Fluoride. The Eluent used must have an affinity to the separated ^{18}F-Fluoride that is stronger than the affinity of the separator.

14

We claim:

1.   An apparatus used in generating Fluoride-18 comprising:

       a material enclosing a chamber volume, wherein said material adsorbs Fluoride-18 formed by beam irradiation of a conversion substance; and

5   an adsorption affecting arrangement, operatively connected to said material, wherein said arrangement affects said material so as to increase or decrease said material's adsorption of Fluoride-18.

2.   An apparatus according to claim 1, wherein said material is stainless steel.

3.   An apparatus according to claim 1, wherein said material is glassy carbon.

10   4.   An apparatus according to claim 1, wherein said material is glassy quartz.

5.   An apparatus according to claim 1, wherein said material is niobium.

6.   An apparatus according to claim 1, wherein said material is molybdenum.

7.   An apparatus according to claim 1, wherein said material is synthetic diamond.

8.   An apparatus according to claim 1, wherein said conversion substance is gaseous ^{18}O, or

15   gaseous ^{16}O, or a compound containing ^{18}O or ^{16}O.

9.   An apparatus according to claim 1, wherein said conversion substance is ^{20}Ne, ^{21}Ne, ^{22}Ne, or a compound containing ^{20}Ne, ^{21}Ne, or ^{22}Ne.

10.   An apparatus according to claim 1, wherein said arrangement cools said material.

11.   An apparatus according to claim 1, wherein said arrangement heats said material.

20   12.   An apparatus according to claim 1, wherein said arrangement provides an electric potential to said material.

13.   An apparatus according to claim 4, wherein said arrangement additionally heats and/or cools said material.

14.   A method for producing ^{18}F-Fluoride comprising the steps:

25   obtaining a conversion substance, wherein said conversion substance produces Fluoride-18

when beam irradiated;

obtaining a material that encloses a chamber volume, wherein said material adsorbs Fluoride-18 formed by beam irradiation of said conversion substance;

placing said conversion substance into said chamber volume;

5   operatively attaching an adsorption affecting arrangement, wherein said arrangement increases or decreases said materials adsorption of Fluoride-18; '

beam irradiating said conversion substance for a predetermined time, wherein said arrangement is used to increase said material's adsorption of Fluoride-18 ;

removing excess said conversion substance; and

10   removing the adsorbed Fluoride-18 from said material, wherein said arrangement is used to decrease said material's adsorption of Fluoride-18.

15.   A method according to claim 14, wherein said material is stainless steel.

16.   A method according to claim 14, wherein said material is glassy carbon.

17.   A method according to claim 14, wherein said material is glassy quartz.

15   18.   A method according to claim 14, wherein said material is niobium.

19.   A method according to claim 14, wherein said material is molybdenum.

20.   A method according to claim 14, wherein said material is synthetic diamond.

21.   A method according to claim 14, wherein said conversion substance is gaseous ^{18}O, or gaseous ^{16}O, or a compound containing ^{18}O or ^{16}O.

20   22.   A method according to claim 14, wherein said conversion substance is ^{20}Ne, ^{21}Ne, ^{22}Ne, or a compound containing ^{20}Ne, ^{21}Ne, or ^{22}Ne.

23.   A method according to claim 14, wherein said arrangement cools said material.

24.   A method according to claim 14, wherein said arrangement heats said material.

25.   A method according to claim 14, wherein said arrangement provides an electric potential to
25   said material.

FIG. 1

100

Beam
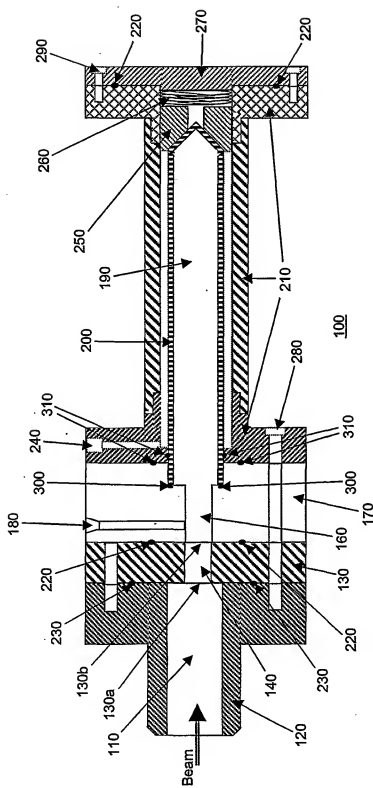
S1010:   Evacuate the chamber volume.

S1020:   Fill the chamber volume with a conversion substance.

S1030:   Irradiate the conversion substance in the chamber volume with protons; ^{18}F-Fluoride is formed and adheres to an accumulation component.

S1040:   Remove the unused conversion substance from the chamber volume.

S1050:   Dissolve the ^{18}F-Fluoride adhered to the accumulation component without removing the component from the chamber.

S1060:   Separate the dissolved ^{18}F-Fluoride.

S1070:   Process and remove the separated ^{18}F-Fluoride.

S1080: Dry the chamber volume in preparation for another run.

FIG. 2